

amendment in adherence with 37 C.F.R. §§1.821 to 1.825. This amendment is accompanied by a floppy disk containing the sequences (SEQ ID NOs:1-54) in computer readable form, and a paper copy of the sequence information that has been printed from the floppy disk.

The information contained in the computer readable form (floppy disk) was prepared through the use of the software program "PatentIn" and is identical to that of the paper copy.

This amendment contains no new matter. The amendments to the specification and/or claims are to provide a formal sequence listing and/or to provide appropriate cross-references to SEQ ID Numbers in accordance with 37 C.F.R. §§1.821 to 1.825. The sequence information provided herein finds support in the specification as filed. Applicants note that amino acid 6 of SEQ ID NO:1 is changed herein from Leu to Val. This change corrects the sequence of AGRP.

If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (510) 337-7871.

LAW OFFICES OF JONATHAN ALAN QUINE  
P.O. BOX 458  
Alameda, CA 94501  
Tel: 510 337-7871  
Fax: 510 337-7877

Respectfully submitted,



Tom Hunter  
Attorney for Applicant(s)  
Reg. No: 38,498

## APPENDIX A

### VERSION WITH MARKINGS TO SHOW CHANGES MADE IN 09/851,586 WITH ENTRY OF THIS AMENDMENT

#### In the specification:

Page 4, line 31 through page 5, line 2:

In certain embodiments,  $X^1X^2X^3X^4X^5X^6$  is VRLHES (SEQ ID NO:6), or conservative substitutions thereof, and/or  $X^7X^8X^9X^{10}X^{11}X^{12}$  is LGQQVP (SEQ ID NO:7), or conservative substitutions thereof, and/or  $X^{14}X^{15}X^{16}$  is RFF (SEQ ID NO:8), or conservative substitutions thereof. In certain embodiments,  $X^{13}$  is not a cysteine and in particularly preferred embodiments,  $X^{13}$  is A.

Page 22, lines 12-31:

--In particularly preferred embodiments, mini-ARGP are represented by formula

#### I (SEQ ID NO:9):



where  $X^1, X^2, X^3, X^4, X^5, X^6, X^7, X^8, X^9, X^{10}, X^{11}, X^{12}, X^{13}, X^{14}, X^{15}$ , and  $X^{16}$  are independently selected amino acids (including natural, synthetic, or modified amino acids); and  $n$  is zero or one. In certain embodiments, in each of the varied domains, one or more of the native residues can be preserved. Thus, for example,  $X^1X^2X^3X^4X^5X^6$  (SEQ ID NO:10) includes, but is not limited to  $VX^2X^3X^4X^5X^6$  (SEQ ID NO:11),  $X^1RX^3X^4X^5X^6$  (SEQ ID NO:12),  $X^1X^2LX^4X^5X^6$  (SEQ ID NO:13),  $X^1X^2X^3HX^5X^6$  (SEQ ID NO:14),  $X^1X^2X^3X^4X^5S$  (SEQ ID NO:15),  $VRX^3X^4X^5X^6$  (SEQ ID NO:16),  $VX^2LX^4X^5X^6$  (SEQ ID NO:17),  $VX^2X^3HX^5X^6$  (SEQ ID NO:18),  $VX^2X^3X^4EX^6$  (SEQ ID NO:19),  $VX^2X^3X^4X^5S$  (SEQ ID NO:20),  $X^1RLX^4X^5X^6$  (SEQ ID NO:21),  $X^1RX^3HX^5X^6$  (SEQ ID NO:22),  $X^1RX^3X^4EX^6$  (SEQ ID NO:23),  $X^1RX^3X^4X^5S$  (SEQ ID NO:24),  $X^1X^2LHX^5X^6$  (SEQ ID NO:25),  $X^1X^2LX^4X^5X^6$  (SEQ ID NO:26),  $X^1X^2LX^4EX^6$  (SEQ ID NO:27),  $X^1X^2LX^4X^5S$  (SEQ ID NO:28),  $X^1X^2X^3HEX^6$  (SEQ ID NO:29),  $X^1X^2X^3HX^5S$  (SEQ ID NO:30),  $X^1X^2X^3X^4ES$  (SEQ ID NO:31),  $VRLX^4X^5X^6$  (SEQ ID NO:32),  $VX^2LHX^5X^6$  (SEQ ID NO:33), VRLHES (SEQ ID NO:34) and the like. Similar permutations are available for  $X^7X^8X^9X^{10}X^{11}X^{12}$  (SEQ ID NO:35) (e.g. LGQQVP (SEQ ID

NO:36),  $LX^8X^9X^{10}X^{11}X^{12}$  (SEQ ID NO:37),  $X^7GX^9X^{10}X^{11}X^{12}$  (SEQ ID NO:38),  $X^7X^8QX^{10}X^{11}X^{12}$  (SEQ ID NO:39),  $X^7X^8X^9QX^{11}X^{12}$  (SEQ ID NO:40),  $X^7X^8X^9X^{10}VX^{12}$  (SEQ ID NO:41),  $X^7X^8X^9X^{10}X^{11}P$  (SEQ ID NO:42),  $LGX^9X^{10}X^{11}X^{12}$  (SEQ ID NO:43),  $LX^8QX^{10}X^{11}X^{12}$  (SEQ ID NO:44),  $LX^8X^9QX^{11}X^{12}$  (SEQ ID NO:45),  $LX^8X^9X^{10}VX^{12}$  (SEQ ID NO:46),  $LX^8X^9X^{10}X^{11}P$  (SEQ ID NO:47),  $LGQX^{10}X^{11}X^{12}$  (SEQ ID NO:48), and the like).

Similarly, the "RFF" domain can be fully mutated or can retain one or more of the native residues. Thus, for example,  $X^{14}X^{15}X^{16}$  includes RFF (SEQ ID NO:8),  $R^{15}X^{15}X^{16}$  (SEQ ID NO:49),  $X^{14}FX^{16}$  (SEQ ID NO:50),  $X^{14}X^{15}F$ ,  $RFX^{16}$  (SEQ ID NO:51),  $RX^{15}F$  (SEQ ID NO:52),  $X^{15}FF$  (SEQ ID NO:53). In certain preferred embodiments,  $X^{13}$  is not cysteine.--

Delete the paragraph at page 30, lines 19-26, and insert:

--A feature of the subject non-peptide compounds is that they structurally mimic the active loop 3-D conformation when bound by the receptor. By active loop is meant residues 111-116 or Arg-Phe-Phe-Asn-Ala-Phe (SEQ ID NO:[ ]54) of the Agouti Related Protein. More specifically, the subject non-peptide compounds are characterized by substantially structurally mimicking the backbone phi angle of amino acid 113 in AGRP, *i.e.* Phe113 phi = -55.4°, and the  $U_1$ - $U_2$  interatomic distance (see structure below). As the subject compounds substantially structurally mimic the active loop, in 9 of 10 lowest energy structures calculated with distance geometry the following requirements should be met. --

Delete the paragraph at page 30, lines 19-26, and insert:

--Accordingly, one aspect of the invention pertains to a method of treating a disease state in mammals that is alleviated by treatment with a polypeptide having an amino acid sequence:  $CX^1X^2X^3X^4X^5X^6CX^7X^8X^9X^{10}X^{11}X^{12}CCDPX^{13}ATCYCX^{14}X^{15}X^{16}N$  AFC YCR<sub>n</sub> (SEQ ID NO:[ ]9), wherein  $X^1, X^2, X^3, X^4, X^5, X^6, X^7, X^8, X^9, X^{10}, X^{11}, X^{12}, X^{13}, X^{14}, X^{15}$ , and  $n$  is 0 or 1, which method comprises administering to a mammal in need of such a treatment a therapeutically effective amount of the polypeptide, which can be administered, by way of illustration and not limitation, in a liquid formulations or a solid formulations, such as in the form of a pharmaceutically acceptable salt thereof. In one preferred embodiment, the polypeptide has the amino acid sequence: CVRLHESCLGQQVPCC DPAATCYCRFFNAFCYC (SEQ ID NO:3). In certain embodiments, such a disease state can be a wasting syndrome.--